REMARKS

Status of Claims and Statement of Substance of the Interview

In response to the Restriction Requirement in this case, applicant elected without traverse Group I, claim 1-17, 26, 27, and 37.

Claims 18-25 and 28-36 stand withdrawn from consideration.

Claims 8-11 are cancelled herein without prejudice.

In response to the election of species requirement, in the paper submitted July 16, 2009, applicant elected the species comprising an antibody Fab fragment that is modified with a PEG effector molecule, has a light chain constant region having at least 90% identity or similarity to the sequence of SEQ ID NO:2, and wherein the interchain cysteine is at position 127 of the heavy chain. In a telephone interview on March 11, 2010, the undersigned applicants' representative requested that the election of species be changed to the species to that wherein the interchain cysteine is at position 233 of the heavy chain, as in SEQ ID NO:1. The Examiner's agreement with this request is noted with appreciation. Currently pending claims that read on the newly elected species are claims 1-3, 7, 8, 12-17, 26-27, and 37.

Depending claims reading on other species are believed to be patentable, and the rejoinder of those claims is respectfully requested, as set forth in greater detail below.

Response to Rejections

35 U.S.C. 112

Claim 3 stands rejected as being indefinite for failing to recite the numbering system used to identify the position of the heavy chain cysteine. Accordingly, claim 3 is amended to recite the Kabat numbering system, as set forth at page 3 of the specification. It is respectfully submitted that this amendment is sufficient to overcome this ground of rejection. Claims 4-7, which also recite the position of the interchain cysteine on either the light chain or the heavy chain, also are amended herein to recite the Kabat numbering system. The purpose of this amendment is to obviate a rejection on the same grounds when these claims are considered on the merits.

Claims 8 and 9 are rejected as being indefinite with regard to the phrase "at least 90% identity or similarity." Without acquiescing in this ground of rejection, but solely

to advance the prosecution of this case, these claims are cancelled herein without prejudice. Claims 10 and 11 which contain this same limitation also are cancelled herein without prejudice for the same reason. Applicant expressly reserves the right to pursue the subject matter of any of claims 8-11 in one or more continuing applications.

Claim 37 is rejected on the grounds of non-enablement with respect to the phrase "pharmaceutical compositions." Without acquiescing in this ground of rejection, but solely to advance the prosecution of this case, this phrase is amended to "compositions," in accordance with the examiner's suggestion at page 6, line 1 of the office action that the rejection could be overcome by deleting the word "pharmaceutical" from the claim..

35 U.S.C. 102

The rejection of claims 1-3, 8, 9, 12, 13 and 27 as anticipated by Carter et al. (WO 93/06217) is respectfully traversed.

The present invention is directed to Fab antibody fragments in which the heavy chain terminates at the interchain cysteine. Fab antibody fragments differ from Fab' fragments in that Fab' fragments have a hinge region, while Fab fragments do not. See, http://en.wikipedia.org/wiki/File:Engineered _monoclonal_antibodies.svg, copy attached hereto as Exhibit A. It also may be seen in the exhibit that in a Fab or Fab' antibody fragment, the heavy and light chains are linked together with a bond. That bond is the interchain cysteine bond, formed from one cysteine in the light chain and one cysteine in the heavy chain. It further may be seen from the Exhibit that the cysteines that form the light chain-heavy chain bond are not at the ends of either the light chain or the heavy chain. In accordance with the present invention, a Fab (not Fab') antibody fragment is provided, wherein the heavy chain is truncated so that it terminates just at the cysteine that can form a bond with the cysteine in the light chain.

The Action notes that "Carter et al. teach *Fab'* fragments comprising CH1 and CL1 wherein the CH1 is terminated at *hinge* cysteine residue at the C-terminus and wherein the cysteine is [the] at the same position as disclosed by the instant specification based upon Kabat numbering (e.g. see pages 5-7 and pages 11-12 and 19)." (emphasis added) The *Fab'* fragment of Carter is not the same as the *Fab* fragment of the present claims; moreover the *hinge* cysteine of Carter does not exist in the Fab fragment of the

present invention, because the Fab fragment of the present invention has no hinge region. Therefore, Carter et al. does not anticipate the present claims, and it is respectfully requested that this ground of rejection be withdrawn.

35 U.S.C. 103

The rejection of claims 1, 12-17, 26 and 27 as obvious over Carter et al. (WO 93/06217) I n view of Chapman et al. (Nature Biotechnology, 1999 17:780-783) is respectfully traversed.

The fact that Carter teaches *Fab'* fragments having *hinge* regions, neither of which is recited in the instant claims, is discussed above. Chapman et al. also teaches *Fab'* fragments, wherein PEGylation takes place at the cysteine in the *hinge* regions. This is readily seen in Chapman et al. Figure 2, at page 781. This figure shows that the fragment includes a light chain bonded to a heavy chain, with a hinge region extending beyond the bond, and with a free thiol group at the cysteine residue in the hinge region. The maleimide group on the PEG molecule binds to the thiol of the hinge region cysteine.

The Fab fragments of the present claims do not have the hinge region, or a cysteine residue in the hinge region. There is no teaching in either Carter et al., or Chapman et al. or the combination of the two, that would lead one skilled in the art to truncate the heavy chain of a Fab fragment right at the cysteine on the heavy chain that forma a bond with the light chain.

Accordingly, the combination of these two references does not render the claimed invention obvious.

Rejoinder of claims to other species

As shown above, generic claim 1 is patentable over the cited references. It is therefore proper to rejoin and examine claims 4-7, directed to species wherein the interchain cysteine of the heavy chain is located at different position on the chain. Favorable consideration is requested.

CONCLUSION

It is respectfully submitted that the rejections have been overcome, and a Notice of Allowance with respect to claims 1-7, 12-17, 26, 27, and 37 is requested. If the Examiner believes that a telephone conference would facilitate examination of the application, the Examiner is invited to call the undersigned applicants' representative at the telephone number indicated below.

Respectfully submitted,

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